IDS/#2 \$ 3/9/02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

SCHUPPAN et al.

Art Unit: 1644

Serial No. TO BE ASSIGNED

Examiner: Ewoldt

Filed: WITH DIVISIONAL APPLN.

For: USE OF ENDOTHELIN INHIBITORS FOR TREATMENT OR PREVENTION OF

FIBROTIC DISORDERS

Hon. Commissioner of Patents and Trademarks Washington, D.C. 20231

INFORMATION DISCLOSURE STATEMENT

Sir:

This subject Information Disclosure Statement is submitted in connection with applicants' continuing duty of disclosure under 37 CFR 1.56.

Listing of Relevant Documents

The relevant documents are listed in the attached Form PTO-1449.

Respectfully submitted,

KEIL & WEINKAUF

Jason D. Voight

Reg. No. 42,205

1101 Connecticut Avenue, N.W. Washington, D.C. 20036 (202) 659-0100

JDV/kas

- in rat biliary liver cirrhosis. 4th International Symposium on Cellular Signal Recognition and Transduction, Berlin, 8.-10.10. 1998, P8.
- 370.Rühl M, Johannsen M, Atkinson J, Manski E, Sahin E, Schuppan D (1998). Soluble collagen type VI induces tyrosine-phosphorylation of paxillin and focal adhesion kinase and activates the MAP kinase erk2 in fibroblasts. 4th International Symposium on Cellular Signal Recognition and Transduction, Berlin, 8.-10.10. 1998, P9.
- 371.Rühl M, Sahin E, Johannsen M, Riecken EO, Schuppan D (1998). Soluble collagen VI drives serum-starved fibroblasts through S-phase and prevents apoptosis via downregulation of BAX. 4th International Symposium on Cellular Signal Recognition and Transduction, Berlin, 8.-10.10. 1998, P10.
- 372. Sedlaczek N, Herbst H, Neuhaus P, Bechstein WO, Riecken EO, Schuppan D (1998). Clusterlike overexpression of insulin-like growth factor II (IGF II) RNA in hepatitis B and C induced liver cirrhosis. 4th International Symposium on Cellular Signal Recognition and Transduction, Berlin, 8.-10.10. 1998, P22.
- 373.Rühl M, Somasundaram R, Tiling N, Schmid M, Ackermann, Riecken EO, Schuppan D (1998). Identification of interleukin 2 (IL-2) as a collagen-binding cytokine. 4th International Symposium on Cellular Signal Recognition and Transduction, Berlin, 8.-10.10. 1998, P13.
- 374.Cho JJ, Jia JD, Boigk G, Hocher B, Rühl M, Somasundaram R, Riecken EO, Schuppan D (1999). Hemmung der hepatischen Kollagenakkumulation bei Ratten mit sekundär biliärer Zirrhose durch niedrig dosierten Endothelin-A-Rezeptorantagonisten LU 135252. Z. Gastroenterol. 37, 61.
 - 375. Schäfer B, Somasundaram R, Schmid M, Rühl M, Riecken EO, Schuppan D (1999). Oncostatin M bindet an die Leberkollagene I, III und VI. Z. Gastroenterol. 37, 67.
 - 376.Rühl M, Atkinson J, Ackermann R, Sahin E, Johannsen M, Riecken EO, Schuppan D (1999). Auto/parakrine Wachstumsstimulierung humaner Sternzellen durch lösliches Kollagen VI. Z. Gastroenterol. 37, 67.
 - 377. Hennig G, Rangs S, Fiebelkorn S, Muthen P, Kroll W, Schuppan D, Voelker M (1999). A microtiter plate sandwich immunoassay for human serum collagen XIV (undulin) and its application for liver fibrosis assessment. Clin. Chem.
 - 378. Albrecht D, Germer CT, Pelz J, Isbert C, Ritz J, Schuppan D, Buhr HJ (1999). Die Laser-induzierte Thermotherapie zur Behandlung von Lebermetastasen: Effizienzsteigerung des thermischen Effektes durch intraarterielle Applikation von Stärkemikrosphären im Rattenmodell. Z. Gastroenterol. 37, 87.
 - 379.Isbert C, Germer CT, Thomsen-Mundt K, Schuppan D, Somasundaram R, Buhr HJ (1999). Überexpression von B7-1 und B7-2 positiven Lymphozyten entlang der Invasionsfront kolorektaler Lebermetastasen-Bedeutung für die Metastasierung? Z. Gastroenterol. 37, 102.
 - 380.Herold C, Gailer B, Schneider HT, Schuppan D, Hahn EG (1999). Dient die Induzierbarkeit der mikrosomalen Leberfunktion zur Differenzierung zirrhotischer Patienten mit kompensierter vs. schwer beeinträchtigter Leberfunktion? Z. Gastroenterol. 37, 104.

- 395.Cramer T, Schuppan D, Riecken EO, Rosewicz S (1999). Thrombospondin-1 is overexpressed by mesenchymal cells in human pancreatic adenocarcinoma. Gastroenterology 118, A1116.
- 396.Cho JJ, Hocher B, Herbst H, Jia JD, Ruehl M, Somasundaram R, Riecken EO, Schuppan D (1999). Suppression of highly activated endothelin/endothelin A receptor system in rat bliary fibrosis blocks collagen accumulation by downregulation of procollagen I and TIMP-1 mRNA. Gastroenterology 118, A1196.
 - 397.Cho JJ, Jia JD, Hocher B, Boigk G, Hahn EG, Riecken EO, Schuppan D (1999). Silymarin downregulates the activated endothelin-system in rat biliary fibrosis. Gastroenterology 118, A1196.
 - 398. Herold C, Reck T, Ott R, Fischler P, Schneider HAT, Schuppan D, Hahn EG (1999). 10 years follow-up in patients with hepatocellular carcinoma. Gastroenterology 118, A1220.
 - 399.Herold C, Heinz R, Radespiel-Troger, Schneider HAT, Schuppan D, Hahn EG (1999). Quantitative testing of liver function in relation to fibrosis in patients with chronic hepatitis B and C. Gastroenterology 118, A1220.
 - 400.Herold C, Heinz R, Radespiel-Troger, Schneider HAT, Schuppan D, Hahn EG (1999). Quantitative liver function in patients with HCV cirrhosis as a predictor of disease progression. Gastroenterology 118, A1220.
 - 401. Isbert C, Thompson-Mundt K, Ruehl M, Schuppan D, Buhr HJ (1999). Expression of B7-1 and B7-2 is increased along invasive margins of colorectal liver metastasis. Gastroenterology 118, A1223.
 - 402 Jia JD, Boigk G, Bauer M, Ruehl M, Strefeld T, Somasundaram R, Milani S, Cho JJ, Riecken EO, Schuppan D (1999). Pentoxifylline potently lowers procollagen α1(I) but increases TIMP-1 mRNA in rat biliary cirrhosis. Gastroenterology 118, A1227.
 - 403. Jia JD, Ruehl M, Bauer M, Strefeld T, Hahn EG, Riecken EO, Schuppan D (1999). Pentoxifylline profoundly downregulates enhanced hepatocyte collagen XVIII/endostatin RNA in rat secondary biliary cirrhosis. Gastroenterology 118, A1227.
 - 404.Rühl M, Wiecher D, Sahin E, Somasundram R, Riecken EO, Schuppan D (1999). Soluble collagen VI as an auto/paracrine inhibitor of apoptosis in hepatic stellate cells. Gastroenterology 118, A1269.
 - 405. Somasundram R, Ruehl R, Oesterling C, Schmid, Riecken EO, Schuppan D (1999). Retention of gelatinases (MMP-2 and -9) by collagen I, III, IV, and of interstitial collagenases (MMP-1 and -8) by collagen VI in the hepatic extracellular matrix. Gastroenterology 118, A1279.
 - 406. Schoepper H, Riecken EO, Hahn EG, Schuppan D (1999). Tissue levels of MMP-1, -2, and TIMP-1 protein in chronic hepatitis: inappropriate balance in biliary fibrosis. Gastroenterology 118, A1351.
 - 407. Jia JD, Sedlaczek N, Bauer M, Wiecher D, Boigk G, Cho JJ, Ruehl M, Hahn EG, Riecken EO, Schuppan D (1999). Expression pattern of connective tissue growth factor in acute and chronic liver fibrogenesis. Hepatology 30: 330A.
 - 408. Cho JJ, Jia JD, Orzechowski HD, Ruehl M, Somasundaram R, Hocher B, Riecken EO, Schuppan D (1999). Endothelin-converting enzyme expression is downregulated in acute and chronic liver injury and fibrogenesis. Hepatology 30: 491A.